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FILING OR 371 DRAWINGS TOT CLMS IND CLMS FIL FEE REC'D ATTY.DOCKET NO ART UNIT APPL NO. (c) DATE 8 23 32 58777.000012 1386 08/18/2003 1653 10/642.272

CONFIRMATION NO. 3248

HUNTON & WILLIAMS LLP Suite 1200 1900 K Street, N.W. Washington, DC 20006-1109 FILING RECEIPT

OC000000012729848

Date Mailed: 05/20/2004

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Applicant(s)

Fumiyuki Hattori, Osaka, JAPAN; Keijiro Sugimura, Osaka, JAPAN; Mayumi Furuya, Osaka, JAPAN;

Assignment For Published Patent Application

DAIICHI SUNTORY PHARMA CO., LTD., Tokyo, JAPAN; DAIICHI SUNTORY BIOMEDICAL RESEARCH, LTD., Osaka, JAPAN;

Domestic Priority data as claimed by applicant

This application is a CON of PCT/JP02/01358 02/18/2001

Foreign Applications

JAPAN 41003/2001 02/16/2001

If Required, Foreign Filing License Granted: 05/20/2004

Projected Publication Date: To Be Determined - pending completion of Sequence Disclosures

Non-Publication Request: No

Early Publication Request: No

Title

Therapeutic methods and agents for diseases associated with decreased expression of AOP-1 gene or AOP-1

Preliminary Class

435

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APPLICATION NUMBER

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ATTORNEY DOCKET NUMBER

10/642,272

HUNTON & WILLIAMS LLP

Washington, DC 20006-1109

1900 K Street, N.W.

08/18/2003

Fumiyuki Hattori

58777.000012

CONFIRMATION NO. 3248

Date Mailed: 05/20/2004

FORMALITIES LETTER

OC000000012729849

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

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1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

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ATTORNEY DOCKET NUMBER

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HUNTON & WILLIAMS LLP

Washington, DC 20006-1109

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08/18/2003

Fumiyuki Hattori

58777.000012

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The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 101642,272
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Date Processed by STIC: 8-28-03

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ERROR DETECTED	SUGGESTED CORRECTION SERIAL NUMBER: 101642127
ATTN: NEW RULES CASES:	Please disregard english "alpha" headers, which were inserted by Pto Software
Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
2Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.
3Misaligned Amino Numbering	The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
4Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
5Variable Length	Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a slugle residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
6PatentIn 2.0 "bug"	A "bug" in Patentin version 2.0 has caused the <220><223> section to be missing from amino acid sequences(s) Normally, Patentin would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220><223> section to the subsequent amino acid sequence. This applies to the mandatory <220><223> sections for Artificial or Unknown sequences.
7Skipped Sequences (OLD RULES)	Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (1) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
8 Skipped Sequences (NEW RULES)	This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences. Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence. 210> sequence id number 400> sequence id number 000
9Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa; and which residue n or Xaa represents.
10lnvalid <213> Response	Per 1.823 of Sequence fules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
11Use of <220>	Sequence(s) missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
Patentin 2.0 "bug"	Please do not use "Copy to Disk" function of PatemIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
13Misuse of n	n can only be used to represent a single nucleotide in a nucleic acid sequence. N is not used to represent any value not specifically a nucleotide.

AMC/MH - Biotechnology Systems Branch - 08/21/2001



OIPE

RAW SEQUENCE LISTING

DATE: 08/28/2003

PATENT APPLICATION: US/10/642,272

TIME: 10:52:52

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3 <110> APPLICANT: Brandt, Kevin S.
             Gaines, Patrick J.
             Stinchcomb, Dan T.
     5
             Wisnewski, Nancy
     8 <120> TITLE OF INVENTION: FLEA HEAD, NERVE CORD, HINDGUT AND MALPIGHIAN TUBULE NUCLEIC
ACID
             MOLECULES, PROTEINS AND USES THEREOF
     9
    11 <130> FILE REFERENCE: FC-8-C2-PCT
C--> 13 <140> CURRENT APPLICATION NUMBER: US/10/642,272
                                                            Does Not Comply
C--> 14 <141> CURRENT FILING DATE: 2003-08-18
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    17 <151> PRIOR FILING DATE: 2001-10-10
                                                                 P.3,6-7
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                                                                         240
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                                                                         480
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DATE: 08/28/2003 TIME: 10:52:52

PATENT APPLICATION: US/10/642,272

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DATE: 08/28/2003 TIME: 10:52:52

PATENT APPLICATION: US/10/642,272

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	165	agtattttat aaattttaat ttgaagcatt cctttatagg tttggaaatt atattttac	240
	167	aaaaaaaaat aaccegteca attgatttta aacaaaacca taaaaaacta ggtgctatag	300
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	171	gcctatccat taatgactta agacttttta gaaatgtttt atatatacat atgtatgcta	420
	173	gatatttaga tggtgtcttg taattgaatt agatttacaa ggaaccaaat gttctacatt	480
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		2210\ CEO TD NO+ 6	
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PATENT APPLICATION: US/10/642,272

DATE: 08/28/2003 TIME: 10:52:52

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		<211> LENGTH: 549					
		<212> TYPE: DNA					
		<213> ORGANISM: Ctenocephalides felis					
	248	<400> SEQUENCE: 9					
	249	aaggatggag tcactgtagc gaagggtatt gatctcaagg acaaatttca gaatattggg	60				
	251	gecaaattag tecaagatgt agetaataac accaatgaag aagetggtga tggtactact	120				
	253	actgctactg tgcttgccag agctattgca aaggaaggct ttgaaaaaaat atctaaagga	180				
	255	gcaaatccca ttgaaatcag acgaggtgtt atgctggctg ttgatgcagt caaagaatct	240				
	257	ttgaaaggaa tgtcgaagcc tgttactacc ccggaggaaa ttgcacaagt tgctaccatt	300				
	259	totgocaatg qaqacaaaqo tattggaaaa ttgatotoag atgocaatgaa gogtgttgga	360				
	261	aaggaaggtg taataacggt taaagatgga aaaactttac atgatgaact tgaggtcatt	420				
	263	gagggcatga agtttgatag aggatcattt caccttactt tatgaattcc agcaaaggtg	480				
	265	ctaaagtaga attocaagat cottattttg toagtgacaa aaaatactca gtcaagcata	540				
		ttctgcttg	549				
		<210> SEQ ID NO: 10					
		<211> LENGTH: 549					
	272	<212> TYPE: DNA					
	273	<213> ORGANISM: Ctenocephalides felis					
		<220> FEATURE:					
	277	<221> NAME/KEY: misc feature .					
	278	<222> LOCATION: (207)(207)					
	279	<223> OTHER INFORMATION: n = unknown at position 207					
		<220> FEATURE:					
	282	<221> NAME/KEY: misc_feature					
	283	<222> LOCATION: (513)(513)					
	284	$\langle 223 \rangle$ OTHER INFORMATION: n = unknown at position 513					
	286	<220> FEATURE:					
•	287	<221> NAME/KEY: misc_feature					
		<222> LOCATION: (515)(515)					
	289	<223> OTHER INFORMATION: n = unknown at position 515					
	291	<400> SEQUENCE: 10					
	292	acgccaggct atgcttcaag ccaccaagga tgccaacaag aagggcccca acttcaccat	60				
	294	caccaaaaag gacagcaact tcaacatgtc ttctgcccaa attgaaagaa acaagaccaa	120				
	296	ggaacaattg gaagaggaaa agaaaatttc tctgtccttc cgtatcaagc ctctggatat	180				
W>	298	cgaatetett ageqttqaaa aaeteanaca aaaggeeaat gaaetttggg aatgeategt	240				
	300	caaqttqqaa actgagaaat acgatctgga ggaacgccaa aaacgccagg actacgatct	300				
	302	taaagaattg aaagaaaggc agaaacaaca actcagacac aaagcattga agaaaggatt	360				
	304	ggatccagaa gccctcacag gaaaatccca cccaaaatcc aagtcgctcc aaatatgaga	420				
	306	gacgtgtcgc acaagatcat atgatgataa gaaaaaatta tttgaaggcg gttcgcacat	480				
	308	tgtctctgaa gtaatgaaaa gtctggaaca gcntncaact attcagaaac gtagtaaact	540				
		agettetaa	549				
		<210> SEQ ID NO: 11					
	314	<211> LENGTH: 87					

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		·	
		<212> TYPE: DNA	
	316	<213> ORGANISM: Ctenocephalides felis	
	318	<400> SEQUENCE: 11	
	319	aatttccagc gcgctcagta ccaccacgtc gagacgatca accgatgcgc ctttcgaacc	60
	321	ccagttagcg tactggttgg cgctgat	87
		<21.0> SEQ ID NO: 12	
		<211> LENGTH: 268	
	326	<212> TYPE: DNA	
		<213> ORGANISM: Ctenocephalides felis	
		<220> FEATURE:	
	331	<221> NAME/KEY: misc_feature	
	332	<222> LOCATION: (30)(31)	
	333	<223> OTHER INFORMATION: n = unknown at positions 30 and 31	
		<400> SEQUENCE: 12	
W>	336	acggtttaca ccctagtcgc gcctaaagan nttttattta aaaacaaatt gtattacttt	60
N>	338	taacaagttt ctctacaaat ttgagaaaac catgttgtat ttttaactac tagtgtaata	120
	240	tttttgttaa aatatattat ttttgtctgt cccaaacgaa tgattttcct gcggccctgc	180
	340	ctgttgcaga tattcctaca cacgttatta taagtcacgc tgtttgcgcg ccgtagcaat	240
	342	ctgttgcaga tattcctaca cacgitatta taagtcacge tgtttgcgcg cogougeant	268
		tacgegeece gttegegeeg ttegttgt	
		<210> SEQ ID NO: 13	
		<211> LENGTH: 436	
		<212> TYPE: DNA	
	350	<213> ORGANISM: Ctenocephalides felis	
	352	<400> SEQUENCE: 13	
	353	attttaaatt ttttataaaa ataatattta aaattataaa aaatatgaaa taatgattaa	60
	355	attagtataa tataatttat tgataatatt aaattgttag gtttattta	120
	357	aaatataata ttoacotgtt taacaaaaac atgtottttt gaaaataata taaagtotaa	180
	359	totgoccatt gaagatttaa aaggoogoag taatttgact gtgcaaaggt agcataatca	240
	361	atagttttt aattgaaagc tggaatgaat gattgaatga aatattaact gtcttaataa	300
	363	aattyttata gaatttaatt tttatyttaa aaagcytaaa tattattaaa ggacgagaag	360
	363	accetttaaa gttttatata taaatataga ttattttaag aatattatta aatttatta	420
			436
		tattaatata tttatt	
		<210> SEQ ID NO: 14	
		<211> LENGTH: 324	
		<212> TYPE: DNA	
		<213> ORGANISM: Ctenocephalides felis	
	375	<400> SEQUENCE: 14	60
	376	accttgaata gtaataatta tototttoag gaccoccatt togaatcaat attataatta	60
	378	aaccttctac tttcagtgct gatgtatcct ttatctatat atatgcaatt agcaattgta	120
	380	reatttatat ataaatgtgt atactttcgt aggttatggt agcgcatttc cacattatcc	180
	382	aattttaagt tcacaaaagt ctctaatgta agtcgtgtct tgtgtgtttc gtagagaatt	240
	307	tagtcggaca attgtaaaat gtcaaataga cttgtaaaag acaaagttat gtagtggttc	300
	205	taaagtagtg atattgtgtc gagt	324
		<210> SEQ ID NO: 15	
		<211> LENGTH: 391	
		<212> TYPE: DNA	
		<213> ORGANISM: Ctenocephalides felis	
		<220> FEATURE:	
	396	<221> NAME/KEY: misc_feature	

RAW SEQUENCE LISTING ERROR SUMMARY

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Input Set : C:\CRF4\Datahold\FC-8-C2-PCT.txt Output Set: N:\CRF4\08282003\J642272.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

```
Seq#:3; N Pos. 129,154,296,316,475
Seq#:7; N Pos. 143,167
Seq#:8; N Pos. 475
Seq#:10; N Pos. 207,513,515
Seq#:12; N Pos. 30,31
Seq#:15; N Pos. 385
Seq#:16; N Pos. 100,123,132,162,178,182,184,248,286,342,403
Seq#:17; N Pos. 399,448,462,486
Seq#:24; N Pos. 230,334,394,459
Seq#:26; N Pos. 403
Seq#:27; N Pos. 445
Seq#:28; N Pos. 422,479,520
Seq#:29; N Pos. 185,258,283
Seq#:31; N Pos. 2,216,332,406,463,467
Seq#:33; N Pos. 344
Seq#:34; N Pos. 403
Seq#:36; N Pos. 445,451
Seq#:38; N Pos. 286
Seq#:39; N Pos. 426
Seq#:45; N Pos. 488
Seq#:54; N Pos. 581
Seq#:57; N Pos. 496
Seq#:59; N Pos. 61,69
Seq#:60; N Pos. 62
Seq#:62; N Pos. 194,248,279
Seq#:63; N Pos. 5,15,16,20,24,29,31,43,48,55,127
Seq#:65; N Pos. 4,12,19,22,41,74,82,107,216,252,298,450
Seq#:67; N Pos. 30,73
Seq#:70; N Pos. 49,71
Sea#:71; N Pos. 207,227,304
Seq#:74; N Pos. 108,284
Seg#:75; N Pos. 108,284
Seq#:76; N Pos. 39,61,182
Seq#:77; N Pos. 436,442
Seq#:78; N Pos. 13,67
Seg#:79; N Pos. 55
Seq#:81; N Pos. 11,28,31,72,74,105,128,170,424,457,490
Seg#:83; N Pos. 205
Seq#:84; N Pos. 4,35,156,181,233
Seq#:85; N Pos. 19
Seq#:88; N Pos. 59,365,404,456
Seq#:89; N Pos. 24,50,92,282
Seq#:90; N Pos. 28,66,73
Seq#:91; N Pos. 46,208,223,234,289
```

RAW SEQUENCE LISTING ERROR SUMMARY

PATENT APPLICATION: US/10/642,272

DATE: 08/28/2003 TIME: 10:52:53

Input Set : C:\CRF4\Datahold\FC-8-C2-PCT.txt
Output Set: N:\CRF4\08282003\J642272.raw

Seq#:92; N Pos. 49,59,61,68

Seq#:94; N Pos. 58,243

Seq#:95; N Pos. 38,129,134,164,188,230,239,289,303,307,349,417,419

Seq#:96; N Pos. 493 Seq#:97; N Pos. 30,63 Seq#:98; N Pos. 36,40 Seq#:99; N Pos. 23,24

VERIFICATION SUMMARY

DATE: 08/28/2003

PATENT APPLICATION: US/10/642,272

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```
L:13 M:270 C: Current Application Number differs, Replaced Current Application Number
L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:113 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:120
M:341 Repeated in SeqNo=3
L:184 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (6) SEQUENCE:
L:207 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7 after pos.:120
L:238 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:8 after pos.:420
L:298 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:180
M:341 Repeated in SeqNo=10
L:336 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:12 after pos.:0
L:413 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:15 after pos.:360
L:480 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:16 after pos.:60
M:341 Repeated in SeqNo=16
L:534 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:17 after pos.:360
M:341 Repeated in SeqNo=17
L:696 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:24 after pos.:180
M:341 Repeated in SeqNo=24
L:746 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:26 after pos.:360
L:779 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:27 after pos.:420
L:820 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:28 after pos.:420
M:341 Repeated in SeqNo=28
L:855 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:29 after pos.:180
M:341 Repeated in SeqNo=29
L:912 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:31 after pos.:0
M:341 Repeated in SeqNo=31
L:976 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:33 after pos.:300
L:1009 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:34 after pos.:360
L:1066 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:36 after pos.:420
L:1075 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (37) SEQUENCE:
L:1097 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:38 after pos.:240
L:1132 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:39 after pos.:420
L:1266 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:45 after pos.:480
L:1471 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:54 after pos.:540
L:1583 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (56) SEQUENCE:
L:1613 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:57 after pos.:480
L:1650 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:59 after pos.:60
L:1677 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:60 after pos.:60
L:1731 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:62 after pos.:180
M:341 Repeated in SeqNo=62
L:1795 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:63 after pos.:0
M:341 Repeated in SeqNo=63
L:1894 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:65 after pos.:0
M:341 Repeated in SeqNo=65
L:1941 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:67 after pos.:0
M:341 Repeated in SeqNo=67
L:2017 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:70 after pos.:0
M:341 Repeated in SeqNo=70
L:2052 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:71 after pos.:180
```

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Input Set : C:\CRF4\Datahold\FC-8-C2-PCT.txt Output Set: N:\CRF4\08282003\J642272.raw

M:341 Repeated in SeqNo=71 L:2112 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:74 after pos.:60 M:341 Repeated in SeqNo=74 L:2142 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:75 after pos.:60 M:341 Repeated in SeqNo=75 L:2175 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:76 after pos.:0 M:341 Repeated in SeqNo=76 L:3752 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (124) SEQUENCE: L:4040 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (134) SEQUENCE: L:4861 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (164) SEQUENCE: L:7893 M:300 W: (50) Intentionally skipped Sequence, : Sequence Id (257) SEQUENCE: